REMARKS

I. Status of the claims and support for the amendments

Claims 7-10, 15, 16, 46, and 47 are cancelled herein.

Claim 28 is currently amended and new claims 48-53 are added.

Claims 28-30 and 48-53 are currently pending.

Support for the amendment of the claims is found at pages 14, 20, and 21 of the Specification and in claims 7-16 and 28-30, as originally filed.

Applicant hereby explicitly reserves the right to pursue any cancelled material in one or more continuation or divisional applications.

II. Response to the Office Action

A. Rejection under 35 U.S.C. §103(a)

Claims 7-10, 15 and 16 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over U.S. Pat. No. 5,244,922 (Burzynski, referred to hereinafter as the '922 patent). In response to this rejection Applicant notes that the rejected claims are cancelled. Accordingly, rejection of these claims is moot and may properly be withdrawn.

Claims 28-30, 46, and 47 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over the '922 patent. The Examiner alleges that the '922 patent demonstrates treatment of neoplastic disease, specifically Hodgkin's disease and that "one skilled in the art would find ample motivation from the prior art [*i.e.* the '922 patent] to employ the prior art combination to treat neoplastic diseases with a reasonable expectation that said combination would be effective to combat said neoplastic diseases including Hodgkin's disease." Applicant respectfully traverses.

MPEP 706.02(j) sets out the criteria which must be met in order to establish obviousness. Section 706.02(j) states, *inter alia*, that:

> [t]o establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991) (emphasis added).

Applicant argues that there is nothing in the cited art which provides motivation to modify the cited reference so as to provide the instantly claimed inventions. There a plurality of differences between the cited patent and the presently claimed invention. These differences include, but are not limited to: 1) the '922 example cited by the Examiner describes the treatment a patient's HIV, not cancer, and used a combination of both Antineoplaston A10 (3-phenylacetylamino-2,6-piperidinedione) and Antineoplaston AS2-1, not AS2-1 alone; and 2) the delivery rate of the pharmaceutical composition is much lower in the '922 patent than in the presently claimed method. In view of these differences, Applicant asserts that there is nothing in the cited reference which provides a motivation for one of skill in the art to modify the invention described in the '922 patent so as to provide instantly claimed method of treating the claimed neoplastic diseases.

The '922 patent is drawn to compositions and methods for treating human viral diseases (*e.g.*, HIV, herpes virus, human papilloma virus, and etc.). As noted, the specific passage cited by the Examiner (Example 2, col. 7, line 45 through col. 8, line 14) describes the treatment of a patient who was suffering from AIDS (as well as Hodgkin's disease). One of ordinary skill in the art would understand Example 2 to provide evidence that the combination of A10 and AS2-1

was effective for ameliorating the AIDS symptoms, specifically the patient's T4 cell count was increasing. Conversely, there is nothing in Example 2 which would lead one of ordinary skill in the art to conclude that AS2-1 alone, or in combination with A10, is an effective treatment for Hodgkin's disease. The fact that the combination therapy described was effective against a virus, such as HIV would not lead one of skill in the art to conclude that the therapy (and certainly not a part of the therapy, the AS2-1) would also effective against a neoplastic disease. This is so because, typically, drugs which are effective anticancer chemotherapeutics are not effective to treat viral disease as well.

Moreover, as indicated the treatment regimen described in Example 2 of the '922 patent is not the regimen which is currently claimed. Example 2 indicates that "Antineoplaston AS2-1, 100 mg/ml infusions were added to the treatment and the dosage of this formulation was gradually increased to 20 g/24h. The treatment was given in the form of **continuous infusions** through an ambulatory pump" ('922 patent, col. 8, ll. 1-4, emphasis added). Even at the maximum dose of 20 g/24 hours the infusion rate would only have been 8.33 ml/hr (*i.e.*, 20g/24h x 10ml/1g = 8.33 ml/hr). In contrast, the currently pending claims are drawn to methods requiring infusion rates of from 100 ml/hr to 400 ml/hr (12 to 48 times the rate described in the '922 patent!).

Thus, Applicant contends that there is nothing in the '922 patent which would lead one of ordinary skill to provide a treatment comprising use of the Antineoplaston AS2-1, alone, rather than in conjunction with Antineoplaston A10, and at an infusion rate of 12-48 times that described in the '922 patent. The '922 patent does nothing to teach or suggest that Antineoplaston AS2-1 would, by itself, be effective against neoplastic disease, nor does it teach that use of high infusion rates would be desirable or effective. Modification is not obvious of the

'922 reference to provide the currently claimed inventions is not taught or suggested by that reference. Consequently, there is nothing in the '922 patent that would motivate one of ordinary skill in the art modify the '922 patent disclosure so as to provide the instantly claimed methods for treatment.

The '922 patent also fails to meet the second requirement set out in MPEP 706.02(j), namely it provides no reasonable expectation that the instantly claimed methods would be successful. There is nothing in the cited reference which indicates that the use of Antineoplaston AS2-1, either alone or in combination with Antineoplaston A10, would provide an effective treatment for neoplastic diseases. Even if the Examiner's interpretation of Example 2 of the '922 patent were taken as accurate (a point that Applicant strongly disputes), that is even if the example were conceded to show treatment of cancer, this would not provide a reasonable expectation of success for the instantly claimed invention.

First, as noted above, Example 2 describes treatment of the patient, who was suffering from AIDS and Hodgkin's disease, using both Antineoplaston A10 and Antineoplaston AS2-1. Second, it describes the delivery rate of AS2-1 as 8.33 ml/hr, at a maximum. Although, Example 2 of the '922 patent indicates that the spleen an liver were no longer enlarged by physical examination, one of ordinary skill in the art would understand that this is not necessarily evidence that the treatment was effective for the treatment of Hodgkin's disease. For example, there is no mention in the example of whether or not the lymph nodes were still enlarged.

Even if the '922 patent was conceded as describing the use of the combination of A10 and AS2-1 to treat cancer, this would not render the presently claimed invention obvious to succeed. That is the instantly claimed invention is not limited to requiring the presence of A10 (nevertheless, due to the "comprising" language of the claims Applicant unequivocally maintains

that the use of A10 in combination with the use of AS2-1, as defined in the pending claims falls within the scope of the claims).

An additional innovative, non-obvious aspect of the instant invention, that clearly distinguishes it from the cited art, is the use of high concentration compositions at high infusion rates (*i.e.*, infusion rates of from 100 to 400 ml/hour).

In order to minimize the toxic side effects associated with chemotherapeutic drugs, it is standard practice to among those of ordinary skill in the art to deliver chemotherapeutic drugs as dilute solutions an in low amounts (to protect the patient's veins) in preference to concentrated solutions in high volumes, during the treatment of cancer. Consequently, one of ordinary skill in the art would be are more likely use the chemotherapeutic agents at lower, rather than higher infusion rates.

Significantly the use of the high infusion rates as disclosed in the instant application produces the unexpected result of increasing urine elimination in patients, thereby decreasing or eliminating the edema which is typically associated with high volume chemotherapeutic treatments. This unexpected diuretic effect is also beneficial in that it provides a mechanism for the elimination of waste products that can otherwise accumulate to toxic levels in the body (see specification page 6, lines 21-26 and page 19, lines 1-6). This diuretic effect is also advantageous because it reduces or eliminates the necessity for the additional use of drugs such as mannitol (which is used to cause increased elimination of fluid in patients who have increased peritumoral edema in the brain) or dexamethasone (which is typically administered to decrease the swelling around brain tumors). Thus the present method obviates the necessity for additional drugs, thereby precluding the possibility of detrimental side effects or toxicity associated with the administration of these additional drugs.

In view of the foregoing, it is Applicant's firm position that the cited art provides no reasonable expectation that the claimed invention could be successfully used for the treatment of the claimed neoplastic diseases.

Finally, Applicant argues that the '922 patent fails the third requirement set out in MPEP 706.02(j) because it does not teach or suggest all of the claimed limitations. For example, there is nothing in the '922 patent which teaches or would suggests delivery of the compositions at an infusion rate of 100 to 400 ml/hour.

In view of the arguments set out above, Applicant believes none of the requirements of MPEP section 706.02(j) have been met. Accordingly, Applicant believes that the rejection of claims 28-30, 46, and 47 has been overcome and that their rejection under 35 U.S.C. §103(a) may now properly be withdrawn. (Applicant notes that claims 46 and 47 are cancelled by the present amendment of the claims. However, much of claim 47 has been incorporated into currently pending claim 28. Applicant asserts that these same arguments also apply to the newly added claims.)

B. Rejection under 35 U.S.C. §112, first paragraph

Claims 28-30 and 46 are rejected under 35 U.S.C. §112, first paragraph as allegedly not being enabled by the Specification. The Examiner specifically alleged that:

> while being enabling for the specific disease or tumor disclosed, does not reasonably provided enablement for term "neoplastic disease" or ..."tumor." The specification does not enable any person skilled in the art to which it pertains...to use the invention commensurate in scope with these claims. The terms "neoplastic disease" in claim[s] 28-30 and "tumor" in claim 46 lack clear exemplary support in the specification as filed.

Applicant respectfully traverses.

As currently amended the claims are now all drawn to methods for treating specifically defined diseases. By not rejecting claim 47 under 35 U.S.C. §112, first paragraph and by

indicating that the Specification is enabling for "specific neoplastic disease," Applicant believes that the Examiner has indicated that methods directed to specific neoplastic diseases set out in the Specification are enabled under §112, first paragraph. Since claim 28, the only independent claim, now recites neoplastic diseases specifically disclosed in the Specification, Applicant believes that the current amendment to the claims overcomes the rejection under 35 U.S.C. §112, first paragraph. Accordingly, this rejection may now properly be withdrawn.

III. Conclusion

In view of the foregoing Amendments and Remarks, Applicant believes that all rejections of the claims have been overcome and may be withdrawn. Accordingly, Applicant respectfully requests reconsideration of the current case and issuance of a "Notice of Allowance" therefor.

The Examiner is invited to contact the undersigned patent agent at (713) 787-1589 with any questions, comments, or suggestions relating to the referenced patent application.

Respectfully submitted,

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